Patent Claims

1. Use of a compound of formula 1

in which

R1 and R2 are both hydrogen or together form an additional bond,

A represents S (sulfur), S(O) (sulfoxide) or S(O)₂ (sulfone),

Ar represents a benzene derivative of formula (a) or (b)

wherein

- R3 is halogen, 1-4C-alkoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,
- R4 is halogen, 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,
- R5 is halogen, 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkyl and

R7 is hydrogen or 1-4C-alkyl,

or wherein

R6 and R7 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or supphur atom,

or a pharmaceutically acceptable salt thereof in the preparation of a pharmaceutical composition for the treatment of neoplasms of lymphoid cells.

2. Use of a compound of formula 1

in which

R1 and R2 are both hydrogen or together form an additional bond,

A represents S (sulfur), S(O) (sulfoxide) or S(O)₂ (sulfone),

Ar represents a benzene derivative of formula (a) or (b)

wherein

- R3 is halogen, 1-4C-alkoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,
- R4 is halogen, 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,
- R5 is halogen, 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkyl and

R7 is hydrogen or 1-4C-alkyl,

or wherein

R6 and R7 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

or a pharmaceutically acceptable salt thereof,

and one or more differentiation inducing agents and/or an agent effective in raising intracellular concentrations of cAMP or a stable analogue of cAMP in the preparation of a pharmaceutical composition for the treatment of neoplasms of lymphoid cells.

3. Use of a compound of formula 1

in which

R1 and R2 are both hydrogen or together form an additional bond,

A represents S (sulfur), S(O) (sulfoxide) or S(O)₂ (sulfone),

Ar represents a benzene derivative of formula (a) or (b)

wherein

- R3 is halogen, 1-4C-alkoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,
- R4 is halogen, 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,
- R5 is halogen, 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkyl and

R7 is hydrogen or 1-4C-alkyl,

or wherein

R6 and R7 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom.

or a pharmaceutically acceptable salt thereof,

and one or more differentiation inducing agents in the preparation of a pharmaceutical composition for the treatment of neoplasms of lymphoid cells.

4. Use of a compound of formula 1

in which

R1 and R2 are both hydrogen or together form an additional bond,

A represents S (sulfur), S(O) (sulfoxide) or S(O)₂ (sulfone),

Ar represents a benzene derivative of formula (a) or (b)

wherein

- R3 is halogen, 1-4C-alkoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,
- R4 is halogen, 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

- R5 is halogen, 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,
- R6 is 1-4C-alkyl and
- R7 is hydrogen or 1-4C-alkyl,

or wherein

R6 and R7 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

or a pharmaceutically acceptable salt thereof,

and an agent effective in raising intracellular concentrations of cAMP or a stable analogue of cAMP in the preparation of a pharmaceutical composition for the treatment of neoplasms of lymphoid cells.

- **5.** Use according to any of the claims 1, 2, 3 or 4 wherein the compound of formula 1 is selected from
- (cis)-4-(2,3-Dihydro-2,2-dimethyl-7-methoxybenzofuran-4-yl)-2-(tetrahydrothiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (cis)-4-(3,4-Dimethoxyphenyl)-2-(1,1-dioxohexahydro-1l⁶-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (cis)-4-(3,4-Dimethoxyphenyl)-2-(1-oxo-hexahydro-1l⁴-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phtha-lazin-1-one,
- (cis)-4-(3-Chloro-4-methoxyphenyl)-2-(tetrahydrothiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one.
- (cis)-4-(3-Chloro-4-methoxyphenyl)-2-(1-oxo-hexahydro-1l⁴-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (cis)-4-(3,4-Diethoxyphenyl)-2-(1,1-dioxohexahydro-1l⁸-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phtha-lazin-1-one,
- (cis)-4-(2,3-Dihydro-2,2-dimethyl-7-methoxybenzofuran-4-yl)-2-(1,1-dioxohexahydro-1l⁸-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aR,8aS)-(cis)-4-(3,4-Dimethoxyphenyl)-2-(1,1-dioxohexahydro-11⁶-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-(cis)-4-(3,4-Dimethoxyphenyl)-2-(1,1-dioxohexahydro-1l⁶-thiopyran-4-yl)-4a,5,8,8a-tetrahy-dro-2H-phthalazin-1-one and
- (cis)-4-(3-Cyclopentyloxy-4-methoxyphenyl)-2-(1,1-dioxohexahydro- $1l^6$ -thiopyran-4-yl)-4a,5,8,8a-tetra-hydro-2H-phthalazin-1-one,
- or a pharmaceutically acceptable salt thereof.
- 6. Use according to any of the claims 1, 2, 3 or 4 wherein the compound of formula 1 is selected from

(cis)-4-(2,3-Dihydro-2,2-dimethyl-7-methoxybenzofuran-4-yl)-2-(tetrahydrothiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,

(4aS,8aR)-(cis)-4-(3,4-Dimethoxyphenyl)-2-(1,1-dioxohexahydro-1l⁶-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one and

(cis)-4-(3-Cyclopentyloxy-4-methoxyphenyl)-2-(1,1-dioxohexahydro-1l⁶-thiopyran-4-yl)-4a,5,8,8a-tetra-hydro-2H-phthalazin-1-one,

or a pharmaceutical acceptable salt thereof.

7. Use of a compound of formula 2

in which

R1 and R2 are both hydrogen or together form an additional bond, R3 represents a benzene derivative of formula (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine, R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is 1-4C-alkyl, $-S(O)_2-R10$, $-S(O)_2-(CH_2)_n-R11$, $-(CH_2)_m-S(O)_2-R12$, -C(O)R13, $-C(O)-(CH_2)_n-R14$, $-(CH_2)_m-C(O)-R15$, Hetaryl, Aryl1 or 1-4C-alkyl-Aryl2,

R10 is 1-4C-alkyl, 5-dimethylaminonaphthalin-1-yl, -N(R16)R17, phenyl or phenyl substituted by R18 and/or R19,

R11 is -N(R16)R17,

R12 is -N(R16)R17,

R13 is 1-4C-alkyl, hydroxycarbonyl-1-4C-alkyl, phenyl, pyridyl, 4-ethyl-piperazin-2,3-dion-1-yl or -N(R16)R17,

R14 is -N(R16)R17,

R15 is -N(R16)R17, phenyl, phenyl substituted by R18 and/or R19 and/or R20,

R16 and R17 are independent from each other hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl,

3-7C-cycloalkylrnethyl, phenyl or phenyl substituted by R18 and/or R19 and/or R20, or R16 and R17 together and with inclusion of the nitrogen atom to which they are bonded, form a 4-morpholinyl-, 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepino- or a 1-piperazinyl-ring of formula (c)

wherein

R21 is pyrid-4-yl, pyrid-4-ylmethyl, 1-4C-alkyl-dimethylamino, dimethylaminocarbonylmethyl, N-methyl-piperidin-4-yl, 4-morpholino-ethyl or tetrahydrofuran-2-ylmethyl,

R18 is halogen, nitro, cyano, carboxyl, 1-4C-alkyl, trifluoromethyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, amino, mono-or di-1-4C-alkylamino, aminocarbonyl 1-4C-alkylamino or mono-or di-1-4C-alkylaminocarbonyl,

R19 is halogen, amino, nitro, 1-4C-alkyl or 1-4C-alkoxy,

R20 is halogen,

Hetaryl is pyrimidin-2-yl, thieno-[2,3-d]pyrimidin-4-yl, 1-methyl-1H-pyrazolo-[3,4-d]pyrimidin-4-yl, thia-zolyl, imidazolyl or furanyl,

Aryl1 is pyridyl, phenyl or phenyl substituted by R18 and/or R19,

Aryl2 is pyridyl, phenyl, phenyl substituted by R18 and/or R19, 2-oxo-2H-chromen-7-yl or 4-(1,2,3-thiadiazol-4-yl)phenyl,

n is an integer from 1 to 4,

m is an integer from 1 to 4,

or a pharmaceutically acceptable salt thereof in the preparation of a pharmaceutical composition for the treatment of neoplasms of lymphoid cells.

8. Use of a compound of formula 2

in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a benzene derivative of formula (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine, R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is 1-4C-alkyl, -S(O)₂-R10, -S(O)₂-(CH₂)_n-R11, -(CH₂)_m-S(O)₂-R12, -C(O)R13, -C(O)-(CH₂)_n-R14, -(CH₂)_m-C(O)-R15, Hetaryl, Aryl1 or 1-4C-alkyl-Aryl2,

R10 is 1-4C-alkyl, 5-dimethylaminonaphthalin-1-yl, -N(R16)R17, phenyl or phenyl substituted by R18 and/or R19,

R11 is -N(R16)R17,

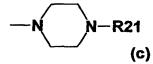
R12 is -N(R16)R17,

R13 is 1-4C-alkyl, hydroxycarbonyl-1-4C-alkyl, phenyl, pyridyl, 4-ethyl-piperazin-2,3-dion-1-yl or -N(R16)R17,

R14 is -N(R16)R17,

R15 is -N(R16)R17, phenyl, phenyl substituted by R18 and/or R19 and/or R20,

R16 and R17 are independent from each other hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl, 3-7C-cycloalkyl-methyl, phenyl or phenyl substituted by R18 and/or R19 and/or R20, or R16 and R17 together and with inclusion of the nitrogen atom to which they are bonded, form a 4-morpholinyl-, 1-pyr-rolidinyl-, 1-piperidinyl-, 1-hexahydroazepino- or a 1-piperazinyl-ring of formula (c)



wherein

R21 is pyrid-4-yl, pyrid-4-ylmethyl, 1-4C-alkyl-dimethylamino, dimethylaminocarbonylmethyl, N-methyl-piperidin-4-yl, 4-morpholino-ethyl or tetrahydrofuran-2-ylmethyl,

R18 is halogen, nitro, cyano, carboxyl, 1-4C-alkyl, trifluoromethyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, amino, mono-or di-1-4C-alkylamino, aminocarbonyl 1-4C-alkylamino or mono-or di-1-4C-alkylaminocarbonyl,

R19 is halogen, amino, nitro, 1-4C-alkyl or 1-4C-alkoxy,

R20 is halogen,

Hetaryl is pyrimidin-2-yl, thieno-[2,3-d]pyrimidin-4-yl, 1-methyl-1H-pyrazolo-[3,4-d]pyrimidin-4-yl, thiazolyl, imidazolyl or furanyl,

Aryl1 is pyridyl, phenyl or phenyl substituted by R18 and/or R19,

Aryl2 is pyridyl, phenyl, phenyl substituted by R18 and/or R19, 2-oxo-2H-chromen-7-yl or 4-(1,2,3-thiadiazol-4-yl)phenyl,

n is an integer from 1 to 4,

m is an integer from 1 to 4,

or a pharmaceutically acceptable salt thereof,

and one or more differentiation inducing agents and/or an agent effective in raising intracellular concentrations of cAMP or a stable analogue of cAMP in the preparation of a pharmaceutical composition for the treatment of neoplasms of lymphoid cells.

9. Use of a compound of formula 2

in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a benzene derivative of formula (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is 1-4C-alkyl, $-S(O)_2$ -R10, $-S(O)_2$ -(CH₂)_n-R11, $-(CH_2)_m$ -S(O)₂-R12, -C(O)-R13, -C(O)-(CH₂)_n-R14, $-(CH_2)_m$ -C(O)-R15, Hetaryl, Aryl1 or 1-4C-alkyl-Aryl2,

R10 is 1-4C-alkyl, 5-dimethylaminonaphthalin-1-yl, -N(R16)R17, phenyl or phenyl substituted by R18 and/or R19,

R11 is -N(R16)R17,

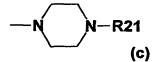
R12 is -N(R16)R17,

R13 is 1-4C-alkyl, hydroxycarbonyl-1-4C-alkyl, phenyl, pyridyl, 4-ethyl-piperazin-2,3-dion-1-yl or -N(R16)R17,

R14 is -N(R16)R17,

R15 is -N(R16)R17, phenyl, phenyl substituted by R18 and/or R19 and/or R20,

R16 and R17 are independent from each other hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl, 3-7C-cycloalkyl-methyl, phenyl or phenyl substituted by R18 and/or R19 and/or R20, or R16 and R17 together and with inclusion of the nitrogen atom to which they are bonded, form a 4-morpholinyl-, 1-pyr-rollidinyl-, 1-piperidinyl-, 1-hexahydroazepino- or a 1-piperazinyl-ring of formula (c)



wherein

R21 is pyrid-4-yl, pyrid-4-ylmethyl, 1-4C-alkyl-dimethylamino, dimethylaminocarbonylmethyl, N-methyl-piperidin-4-yl, 4-morpholino-ethyl or tetrahydrofuran-2-ylmethyl,

R18 is halogen, nitro, cyano, carboxyl, 1-4C-alkyl, trifluoromethyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, amino, mono-or di-1-4C-alkylamino, aminocarbonyl 1-4C-alkylcarbonylamino or mono-or di-1-4C-alkylaminocarbonyl.

R19 is halogen, amino, nitro, 1-4C-alkyl or 1-4C-alkoxy,

R20 is halogen,

Hetaryl is pyrimidin-2-yl, thieno-[2,3-d]pyrimidin-4-yl, 1-methyl-1H-pyrazolo-[3,4-d]pyrimidin-4-yl, thia-zolyl, imidazolyl or furanyl,

Aryl1 is pyridyl, phenyl or phenyl substituted by R18 and/or R19,

Aryl2 is pyridyl, phenyl, phenyl substituted by R18 and/or R19, 2-oxo-2H-chromen-7-yl or 4-(1,2,3-thiadiazol-4-yl)phenyl,

n is an integer from 1 to 4,

m is an integer from 1 to 4,

or a pharmaceutically acceptable salt thereof,

and one or more differentiation inducing agents in the preparation of a pharmaceutical composition for the treatment of neoplasms of lymphoid cells.

10. Use of a compound of formula 2

in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a benzene derivative of formula (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine, R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is 1-4C-alkyl, $-S(O)_2-R10$, $-S(O)_2-(CH_2)_n-R11$, $-(CH_2)_m-S(O)_2-R12$, -C(O)R13, $-C(O)-(CH_2)_n-R14$, $-(CH_2)_m-C(O)-R15$, Hetaryl, Aryl1 or 1-4C-alkyl-Aryl2,

R10 is 1-4C-alkyl, 5-dimethylaminonaphthalin-1-yl, -N(R16)R17, phenyl or phenyl substituted by R18 and/or R19,

R11 is -N(R16)R17,

R12 is -N(R16)R17,

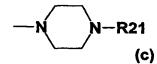
R13 is 1-4C-alkyl, hydroxycarbonyl-1-4C-alkyl, phenyl, pyridyl, 4-ethyl-piperazin-2,3-dion-1-yl or -N(R16)R17,

R14 is -N(R16)R17,

R15 is -N(R16)R17, phenyl, phenyl substituted by R18 and/or R19 and/or R20,

R16 and R17 are independent from each other hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl,

3-7C-cycloalkylmethyl, phenyl or phenyl substituted by R18 and/or R19 and/or R20, or R16 and R17 together and with inclusion of the nitrogen atom to which they are bonded, form a 4-morpholinyl-, 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepino- or a 1-piperazinyl-ring of formula (c)



wherein

R21 is pyrid-4-yl, pyrid-4-ylmethyl, 1-4C-alkyl-dimethylamino, dimethylaminocarbonylmethyl, N-methyl-piperidin-4-yl, 4-morpholino-ethyl or tetrahydrofuran-2-ylmethyl,

R18 is halogen, nitro, cyano, carboxyl, 1-4C-alkyl, trifluoromethyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, amino, mono-or di-1-4C-alkylamino, aminocarbonyl 1-4C-alkylamino or mono-or di-1-4C-alkylaminocarbonyl,

R19 is halogen, amino, nitro, 1-4C-alkyl or 1-4C-alkoxy,

R20 is halogen,

Hetaryl is pyrimidin-2-yl, thieno-[2,3-d]pyrimidin-4-yl, 1-methyl-1H-pyrazolo-[3,4-d]pyrimidin-4-yl, thia-zolyl, imidazolyl or furanyl,

Aryl1 is pyridyl, phenyl or phenyl substituted by R18 and/or R19,

Aryl2 is pyridyl, phenyl, phenyl substituted by R18 and/or R19, 2-oxo-2H-chromen-7-yl or 4-(1,2,3-thiadiazol-4-yl)phenyl,

n is an integer from 1 to 4,

m is an integer from 1 to 4,

or a pharmaceutically acceptable salt thereof,

and an agent effective in raising intracellular concentrations of cAMP or a stable analogue of cAMP in the preparation of a pharmaceutical composition for the treatment of neoplasms of lymphoid cells.

- **11.** Use according to any of the claims 7, 8, 9 or 10 wherein the compound of formula 2 is selected from
- (4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-[1-(toluene-4-sulfonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-(1-methanesulfonyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-2-(1-Acetyl-piperidin-4-yl)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one.
- 5-{4-{(4aS,8aR)-4-(3,4-Diethoxy-phenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-5-oxo-pentanoic acid,
- (4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-[1-(1-pyridin-4-yl-methanoyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- 4-[(4aS,8aR)-4-(3,4-Diethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidine-1-carboxylic acid tert-butylamide,
- 4-[(4aS,8aR)-4-(3,4-Diethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidine-1-carboxylic acid phenylamide,
- 4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidine-1-carboxylic acid tert-butylamide,
- (cis)-4-[4-(7-Methoxy-2,2-dimethyl-2,3-dihydro-benzofuran-4-yl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidine-1-carboxylic acid tert-butylamide,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(5-dimethylamino-naphthalene-1-sulfonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(4-nitro-phenyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-pyridin-4-ylmethyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(morpholine-4-carbonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-2-{1-[2-(4-Amino-3,5-dichloro-phenyl)-2-oxo-ethyl]-piperidin-4-yl}-4-(3,4-dimethoxy-phenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- 4-(3,4-Dimethoxyphenyl)-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-piperidin-4-yl]-4a,5,8,8a-te-trahydro-2H-naphthalen-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-thieno[2,3-d]pyrimidin-4-yl-piperidin-4-yl)-4a,5,8,8a-tetra-hydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-pyrimidin-2-yl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phtha-lazin-1-one,

- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(2-oxo-2H-chromen-7-ylmethyl)-piperidin-4-yl]-4a,5,8,8a-te-trahydro-2H-phthalazin-1-one,
- 4-(3,4-Dimethoxyphenyl)-2-(1-isopropyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one, (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(2-morpholin-4-yl-2-oxo-ethyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-phenethyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one.
- (4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-[1-(morpholine-4-carbonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-pyridin-3-ylmethyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxy-phenyl)-2-(1-pyridin-2-ylmethyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-[1-(2-morpholin-4-yl-ethanoyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-(1-{2-[4-(2-dimethylamino-ethyl)-piperazin-1-yl]-ethanoyl}-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- 2-{4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-N-isopropyl-acetamide,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(4-1,2,3-thiadiazol-4-yl-benzyl)-piperidin-4-yl]-4a,5,8,8a-tetra-hydro-2H-phthalazin-1-one,
- 1-(1-{4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-methanoyl)-4-ethyl-piperazine-2,3-dione,
- 4-(2-{4-[(4aS,8aR)-4-(3,4-Dimethoxy-phenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-ethanoylamino)-benzoic acid ethyl ester and
- 2-{4-{(4aS, 8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-acetamide,
- or a pharmaceutically acceptable salt thereof.
- **12.** Use according to any of the claims 7, 8, 9 or 10 wherein the compound of formula 2 is (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-pyrimidin-2-yl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one or a pharmaceutically acceptable salt thereof.
- **13.** Use according to any of the claims 7, 8, 9 or 10 wherein the compound of formula 2 is (4aS,8aR)-4-(3,4-Dimethoxy-phenyl)-2-(1-pyridin-2-ylmethyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one or a pharmaceutically acceptable salt thereof.
- 14. Use according to any of the claims 7, 8, 9 or 10 wherein the compound of formula 2 is

2-{4-[(4aS, 8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-acetamide or a pharmaceutically acceptable salt thereof.

15. Use of a compound selected from

N-(3,5-dichloropyrid-4-yl)-3-cyclopentyloxy-4-methoxybenzamide [INN: PICLAMILAST],

3-cyclopropylmethoxy-4-diffuoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST], 3-cyclopropylmethoxy-4-diffuoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide),

3-[3-(cyclopentyloxy)-4-methoxybenzyl]-6-(ethylamino)-8-isopropyl-3H-purine [Research Code: V-11294Al.

N-[9-methyl-4-oxo-1-phenyl-3,4,6,7-tetrahydropyrrolo[3,2,1-jk][1,4]benzo-diazepin-3(R)-yl]pyridine-4-carboxamide [Research Code: CI-1018],

3,7-dihydro-3-(4-chlorophenyl)-1-propyl-1H-purine-2,6-dione [INN: AROFYLLINE],

N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281],

N-(3,5-dichloropyridin-4-yl)-2-[5-fluoro-1-(4-fluorobenzyl)-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-343],

Tetrahydro-5-[4-methoxy-3-[(1S,2S,4R)-2-norbornyloxy]phenyl]-2(1H)-pyrimidone [INN: ATIZORAM]; ß-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1,3-dioxo-2H-isoindole-2-propanamide [Research Code: CDC-801],

Methanesulfonic acid 2-(2,4-dichlorophenylcarbonyl)-3-ureidobenzo-furan-6-yl ester [INN: LIRIMI-LAST],

3,5-dichloro-4-[8-methoxy-2-(trifluoromethyl)quinolin-5-ylcarbox-amido]pyridine-1-oxide [Research Code: SCH-351591],

cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast], the compounds with the research codes CDC-998, D-4396, IC-485, CC-1088 and KW4490, or a pharmaceutically acceptable salt thereof in the preparation of a pharmaceutical composition for the treatment of neoplasms of lymphoid cells.

16. Use of a compound selected from

N-(3,5-dichloropyrid-4-yl)-3-cyclopentyloxy-4-methoxybenzamide [INN: PICLAMILAST], 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST], 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide),

3-[3-(cyclopentyloxy)-4-methoxybenzyl]-6-(ethylamino)-8-isopropyl-3H-purine [Research Code: V-11294A],

N-[9-methyl-4-oxo-1-phenyl-3,4,6,7-tetrahydropyrrolo[3,2,1-jk][1,4]benzo-diazepin-3(R)-yl]pyridine-4-carboxamide [Research Code: CI-1018],

3,7-dihydro-3-(4-chlorophenyl)-1-propyl-1H-purine-2,6-dione [INN: AROFYLLINE],

N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281],

N-(3,5-dichloropyridin-4-yl)-2-[5-fluoro-1-(4-fluorobenzyl)-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-343],

Tetrahydro-5-[4-methoxy-3-[(1S,2S,4R)-2-norbornyloxy]phenyl]-2(1H)-pyrimidone [INN: ATIZORAM]; ß-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1,3-dioxo-2H-isoindole-2-propanamide [Research Code: CDC-801],

Methanesulfonic acid 2-(2,4-dichlorophenylcarbonyl)-3-ureidobenzo-furan-6-yl ester [INN: LIRIMI-LAST],

3,5-dichloro-4-[8-methoxy-2-(trifluoromethyl)quinolin-5-ylcarbox-amido]pyridine-1-oxide [Research Code: SCH-351591],

cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast], the compounds with the research codes CDC-998, D-4396, IC-485, CC-1088 and KW4490, or a pharmaceutically acceptable salt thereof,

and one or more differentiation inducing agents and/or an agent effective in raising intracellular concentrations of cAMP or a stable analogue of cAMP in the preparation of a pharmaceutical composition for the treatment of neoplasms of lymphoid cells.

17. Use of a compound selected from

N-(3,5-dichloropyrid-4-yl)-3-cyclopentyloxy-4-methoxybenzamide [INN: PICLAMILAST], 3-cyclopropylmethoxy-4-diffuoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST], 3-cyclopropylmethoxy-4-diffuoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide),

3-[3-(cyclopentyloxy)-4-methoxybenzyl]-6-(ethylamino)-8-isopropyl-3H-purine [Research Code: V-11294A],

N-[9-methyl-4-oxo-1-phenyl-3,4,6,7-tetrahydropyrrolo[3,2,1-jk][1,4]benzo-diazepin-3(R)-yl]pyridine-4-carboxamide [Research Code: CI-1018],

3,7-dihydro-3-(4-chlorophenyl)-1-propyl-1H-purine-2,6-dione [INN: AROFYLLINE],

N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281],

N-(3,5-dichloropyridin-4-yl)-2-[5-fluoro-1-(4-fluorobenzyl)-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-343],

Tetrahydro-5-[4-methoxy-3-[(1S,2S,4R)-2-norbornyloxy]phenyl]-2(1H)-pyrimidone [INN: ATIZORAM]; ß-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1,3-dioxo-2H-isoindole-2-propanamide [Research Code: CDC-801],

Methanesulfonic acid 2-(2,4-dichlorophenylcarbonyl)-3-ureidobenzo-furan-6-yl ester [INN: LIRIMI-LAST],

3,5-dichloro-4-[8-methoxy-2-(trifluoromethyl)quinolin-5-ylcarbox-amido]pyridine-1-oxide [Research Code: SCH-351591],

cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast], the compounds with the research codes CDC-998, D-4396, IC-485, CC-1088 and KW4490, or a pharmaceutically acceptable salt thereof,

and one or more differentiation inducing agents in the preparation of a pharmaceutical composition for the treatment of neoplasms of lymphoid cells.

18. Use of a compound selected from

N-(3,5-dichloropyrid-4-yl)-3-cyclopentyloxy-4-methoxybenzamide [INN: PICLAMILAST], 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST], 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide),

3-[3-(cyclopentyloxy)-4-methoxybenzyl]-6-(ethylamino)-8-isopropyl-3H-purine [Research Code: V-11294A],

N-[9-methyl-4-oxo-1-phenyl-3,4,6,7-tetrahydropyrrolo[3,2,1-jk][1,4]benzo-diazepin-3(R)-yl]pyridine-4-carboxamide [Research Code: Cl-1018],

3,7-dihydro-3-(4-chlorophenyl)-1-propyl-1H-purine-2,6-dione [INN: AROFYLLINE],

N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281],

N-(3,5-dichloropyridin-4-yl)-2-[5-fluoro-1-(4-fluorobenzyl)-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-343],

Tetrahydro-5-[4-methoxy-3-[(1S,2S,4R)-2-norbornyloxy]phenyl]-2(1H)-pyrimidone [INN: ATIZORAM]; ß-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1,3-dioxo-2H-isoindole-2-propanamide [Research Code: CDC-801],

Methanesulfonic acid 2-(2,4-dichlorophenylcarbonyl)-3-ureidobenzo-furan-6-yl ester [INN: LIRIMI- LAST],

3,5-dichloro-4-[8-methoxy-2-(trifluoromethyl)quinolin-5-ylcarbox-amido]pyridine-1-oxide [Research Code: SCH-351591],

cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast], the compounds with the research codes CDC-998, D-4396, IC-485, CC-1088 and KW4490, or a pharmaceutically acceptable salt thereof,

and an agent effective in raising intracellular concentrations of cAMP or a stable analogue of cAMP in the preparation of a pharmaceutical composition for the treatment of neoplasms of lymphoid cells.

19. Use according to any of the claims 15, 16, 17 or 18 wherein the compound is selected from N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281],

cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast], 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST] and

3-cyclopropylmethoxy-4-diffuoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide) or a pharmaceutically acceptable salt thereof.

- 20. Use according to any of the claims 15, 16, 17 or 18 wherein the compound is selected from 3-cyclopropylmethoxy-4-diffuoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST] and 3-cyclopropylmethoxy-4-diffuoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide), or a pharmaceutically acceptable salt thereof.
- 21. Use according to any of the claims 15, 16, 17 or 18 wherein the compound is 3-cyclopropyl-methoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST] or a pharmaceutically acceptable salt thereof.
- 22. Use according to any of the claims 15, 16, 17 or 18 wherein the compound is 3-cyclopropyl-methoxy-4-difluoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide) or a pharmaceutically acceptable salt thereof.
- 23. Use according to any of the claims 15, 16, 17 or 18 wherein the compound is N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281] or a pharmaceutically acceptable salt thereof.
- 24. Use according to any of the claims 15, 16, 17 or 18 wherein the compound is cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast] or a pharmaceutically acceptable salt thereof.
- **25.** A method of treating neoplasms of lymphoid cells in a mammal, comprising administering to said mammal a therapeutically effective amount of a compound of formula 1

in which

R1 and R2 are both hydrogen or together form an additional bond,

A represents S (sulfur), S(O) (sulfoxide) or S(O)₂ (sulfone),

Ar represents a benzene derivative of formula (a) or (b)

wherein

R3 is halogen, 1-4C-alkoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R4 is halogen, 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is halogen, 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkyl and

R7 is hydrogen or 1-4C-alkyl,

or wherein

R6 and R7 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

or a pharmaceutically acceptable salt thereof.

26. A method for treating neoplasms of lymphoid cells in a mammal, including: administering to said mammal therapeutically effective amounts of

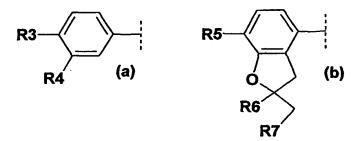
(i) a compound of formula 1

in which

R1 and R2 are both hydrogen or together form an additional bond,

A represents S (sulfur), S(O) (sulfoxide) or S(O)₂ (sulfone),

Ar represents a benzene derivative of formula (a) or (b)



wherein

R3 is halogen, 1-4C-alkoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R4 is halogen, 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is halogen, 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkyl and

R7 is hydrogen or 1-4C-alkyl,

or wherein

R6 and R7 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

or a pharmaceutically acceptable salt thereof,

and (ii) one or more differentiation inducing agents and/or an agent effective in raising intracellular concentrations of cAMP or a stable analogue thereof.

- 27. A method for treating neoplasms of lymphoid cells in a mammal, including: administering to said mammal therapeutically effective amounts of
- (i) a compound of formula 1

in which

R1 and R2 are both hydrogen or together form an additional bond,

A represents S (sulfur), S(O) (sulfoxide) or S(O)₂ (sulfone),

Ar represents a benzene derivative of formula (a) or (b)

wherein

- R3 is halogen, 1-4C-alkoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine.
- R4 is halogen, 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,
- R5 is halogen, 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkyl and

R7 is hydrogen or 1-4C-alkyl,

or wherein

(i) a compound of formula 1

R6 and R7 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

or a pharmaceutically acceptable salt thereof, and (ii) one or more differentiation inducing agents.

28. A method for treating neoplasms of lymphoid cells in a mammal, including: administering to said mammal therapeutically effective amounts of

in which

R1 and R2 are both hydrogen or together form an additional bond,

A represents S (sulfur), S(O) (sulfoxide) or S(O)₂ (sulfone),

Ar represents a benzene derivative of formula (a) or (b)

wherein

R3 is halogen, 1-4C-alkoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R4 is halogen, 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

- R5 is halogen, 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,
- R6 is 1-4C-alkyl and
- R7 is hydrogen or 1-4C-alkyl,

or wherein

R6 and R7 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

or a pharmaceutically acceptable salt thereof,

and (ii) an agent effective in raising intracellular concentrations of cAMP or a stable analogue thereof.

- 29. A method according to any of claims 25, 26, 27 or 28, wherein the compound of formula 1 is selected from
- (cis)-4-(2,3-Dihydro-2,2-dimethyl-7-methoxybenzofuran-4-yl)-2-(tetrahydrothiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (cis)-4-(3,4-Dimethoxyphenyl)-2-(1,1-dioxohexahydro-1l⁶-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (cis)-4-(3,4-Dimethoxyphenyl)-2-(1-oxo-hexahydro-1l⁴-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phtha-lazin-1-one,
- (cis)-4-(3-Chloro-4-methoxyphenyl)-2-(tetrahydrothiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (cis)-4-(3-Chloro-4-methoxyphenyl)-2-(1-oxo-hexahydro-1I⁴-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (cis)-4-(3,4-Diethoxyphenyl)-2-(1,1-dioxohexahydro-1l⁶-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phtha-lazin-1-one,
- (cis)-4-(2,3-Dihydro-2,2-dimethyl-7-methoxybenzofuran-4-yl)-2-(1,1-dioxohexahydro-1l⁸-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aR,8aS)-(cis)-4-(3,4-Dimethoxyphenyl)-2-(1,1-dioxohexahydro-1l⁶-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-(cis)-4-(3,4-Dimethoxyphenyl)-2-(1,1-dioxohexahydro-11⁶-thiopyran-4-yl)-4a,5,8,8a-tetrahy-dro-2H-phthalazin-1-one and
- (cis)-4-(3-Cyclopentyloxy-4-methoxyphenyl)-2-(1,1-dioxohexahydro-1l⁶-thiopyran-4-yl)-4a,5,8,8a-tetra-hydro-2H-phthalazin-1-one,
- or a pharmaceutically acceptable salt thereof.
- **30.** A method according to any of claims 25, 26, 27 or 28, wherein the compound of formula 1 is selected from
- (cis)-4-(2,3-Dihydro-2,2-dimethyl-7-methoxybenzofuran-4-yl)-2-(tetrahydrothiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,

(4aS,8aR)-(cis)-4-(3,4-Dimethoxyphenyl)-2-(1,1-dioxohexahydro-116-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one and

(cis)-4-(3-Cyclopentyloxy-4-methoxyphenyl)-2-(1,1-dioxohexahydro-11⁶-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,

or a pharmaceutically acceptable salt thereof.

31. A method of treating neoplasms of lymphoid cells in a mammal, comprising administering to said mammal a therapeutically effective amount of a compound of formula 2

in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a benzene derivative of formula (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine, R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is 1-4C-alkyl, $-S(O)_2-R10$, $-S(O)_2-(CH_2)_n-R11$, $-(CH_2)_m-S(O)_2-R12$, -C(O)R13, $-C(O)-(CH_2)_n-R14$, $-(CH_2)_m-C(O)-R15$, Hetaryl, Aryl1 or 1-4C-alkyl-Aryl2,

R10 is 1-4C-alkyl, 5-dimethylaminonaphthalin-1-yl, -N(R16)R17, phenyl or phenyl substituted by R18 and/or R19,

R11 is -N(R16)R17,

R12 is -N(R16)R17,

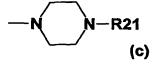
R13 is 1-4C-alkyl, hydroxycarbonyl-1-4C-alkyl, phenyl, pyridyl, 4-ethyl-piperazin-2,3-dion-1-yl or -N(R16)R17,

R14 is -N(R16)R17,

R15 is -N(R16)R17, phenyl, phenyl substituted by R18 and/or R19 and/or R20,

R16 and R17 are independent from each other hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl,

3-7C-cycloalkylmethyl, phenyl or phenyl substituted by R18 and/or R19 and/or R20, or R16 and R17 together and with inclusion of the nitrogen atom to which they are bonded, form a 4-morpholinyl-, 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepino- or a 1-piperazinyl-ring of formula (c)



wherein

R21 is pyrid-4-yl, pyrid-4-ylmethyl, 1-4C-alkyl-dimethylamino, dimethylaminocarbonylmethyl, N-methyl-piperidin-4-yl, 4-morpholino-ethyl or tetrahydrofuran-2-ylmethyl,

R18 is halogen, nitro, cyano, carboxyl, 1-4C-alkyl, trifluoromethyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, amino, mono-or di-1-4C-alkylamino, aminocarbonyl 1-4C-alkylamino or mono-or di-1-4C-alkylaminocarbonyl,

R19 is halogen, amino, nitro, 1-4C-alkyl or 1-4C-alkoxy,

R20 is halogen,

Hetaryl is pyrimidin-2-yl, thieno-[2,3-d]pyrimidin-4-yl, 1-methyl-1H-pyrazolo-[3,4-d]pyrimidin-4-yl, thia-zolyl, imidazolyl or furanyl,

Aryl1 is pyridyl, phenyl or phenyl substituted by R18 and/or R19,

Aryl2 is pyridyl, phenyl, phenyl substituted by R18 and/or R19, 2-oxo-2H-chromen-7-yl or 4-(1,2,3-thiadiazol-4-yl)phenyl.

- n is an integer from 1 to 4,
- m is an integer from 1 to 4, or a pharmaceutically acceptable salt thereof.
- **32.** A method for treating neoplasms of lymphoid cells in a mammal, including: administering to said mammal therapeutically effective amounts of
- (i) a compound of formula 2

in which

R1 and R2 are both hydrogen or together form an additional bond, R3 represents a benzene derivative of formula (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine, R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is 1-4C-alkyl, $-S(O)_2$ -R10, $-S(O)_2$ -(CH₂)_n-R11, $-(CH_2)_m$ -S(O)₂-R12, -C(O)-R13, -C(O)-(CH₂)_n-R14, $-(CH_2)_m$ -C(O)-R15, Hetaryl, Aryl1 or 1-4C-alkyl-Aryl2,

R10 is 1-4C-alkyl, 5-dimethylaminonaphthalin-1-yl, -N(R16)R17, phenyl or phenyl substituted by R18 and/or R19,

R11 is -N(R16)R17,

R12 is -N(R16)R17,

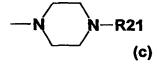
R13 is 1-4C-alkyl, hydroxycarbonyl-1-4C-alkyl, phenyl, pyridyl, 4-ethyl-piperazin-2,3-dion-1-yl or -N(R16)R17,

R14 is -N(R16)R17,

R15 is -N(R16)R17, phenyl, phenyl substituted by R18 and/or R19 and/or R20,

R16 and R17 are independent from each other hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl,

3-7C-cycloalkylmethyl, phenyl or phenyl substituted by R18 and/or R19 and/or R20, or R16 and R17 together and with inclusion of the nitrogen atom to which they are bonded, form a 4-morpholinyl-, 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepino- or a 1-piperazinyl-ring of formula (c)



wherein

R21 is pyrid-4-yl, pyrid-4-ylmethyl, 1-4C-alkyl-dimethylamino, dimethylaminocarbonylmethyl, N-methyl-piperidin-4-yl, 4-morpholino-ethyl or tetrahydrofuran-2-ylmethyl,

R18 is halogen, nitro, cyano, carboxyl, 1-4C-alkyl, trifluoromethyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, amino, mono-or di-1-4C-alkylamino, aminocarbonyl 1-4C-alkylamino or mono-or di-1-4C-alkylaminocarbonyl,

R19 is halogen, amino, nitro, 1-4C-alkyl or 1-4C-alkoxy,

R20 is halogen,

Hetaryl is pyrimidin-2-yl, thieno-[2,3-d]pyrimidin-4-yl, 1-methyl-1H-pyrazolo-[3,4-d]pyrimidin-4-yl, thia-zolyl, imidazolyl or furanyl,

Aryl1 is pyridyl, phenyl or phenyl substituted by R18 and/or R19,

Aryl2 is pyridyl, phenyl, phenyl substituted by R18 and/or R19, 2-oxo-2H-chromen-7-yl or 4-(1,2,3-thiadiazol-4-yl)phenyl,

n is an integer from 1 to 4.

m is an integer from 1 to 4, or a pharmaceutically acceptable salt thereof, and (ii) one or more differentiation inducing agents and/or an agent effective in raising intracellular concentrations of cAMP or a stable analogue thereof.

33. A method for treating neoplasms of lymphoid cells in a mammal, including: administering to said mammal therapeutically effective amounts of(i) a compound of formula 2

in which

R1 and R2 are both hydrogen or together form an additional bond, R3 represents a benzene derivative of formula (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine, R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is 1-4C-aikyl, $-S(O)_2$ -R10, $-S(O)_2$ -(CH₂)_n-R11, $-(CH_2)_m$ -S(O)₂-R12, -C(O)-R13, -C(O)-(CH₂)_n-R14, $-(CH_2)_m$ -C(O)-R15, Hetaryl, Aryl1 or 1-4C-alkyl-Aryl2,

R10 is 1-4C-alkyl, 5-dimethylaminonaphthalin-1-yl, -N(R16)R17, phenyl or phenyl substituted by R18 and/or R19,

R11 is -N(R16)R17,

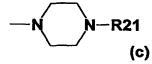
R12 is -N(R16)R17,

R13 is 1-4C-alkyl, hydroxycarbonyl-1-4C-alkyl, phenyl, pyridyl, 4-ethyl-piperazin-2,3-dion-1-yl or -N(R16)R17,

R14 is -N(R16)R17,

R15 is -N(R16)R17, phenyl, phenyl substituted by R18 and/or R19 and/or R20,

R16 and R17 are independent from each other hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl, 3-7C-cyc



wherein

R21 is pyrid-4-yl, pyrid-4-ylmethyl, 1-4C-alkyl-dimethylamino, dimethylaminocarbonylmethyl, N-methyl-piperidin-4-yl, 4-morpholino-ethyl or tetrahydrofuran-2-ylmethyl,

R18 is halogen, nitro, cyano, carboxyl, 1-4C-alkyl, trifluoromethyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, amino, mono-or di-1-4C-alkylamino, aminocarbonyl 1-4C-alkylamino or mono-or di-1-4C-alkylaminocarbonyl,

R19 is halogen, amino, nitro, 1-4C-alkyl or 1-4C-alkoxy,

R20 is halogen,

Hetaryl is pyrimidin-2-yl, thieno-[2,3-d]pyrimidin-4-yl, 1-methyl-1H-pyrazolo-[3,4-d]pyrimidin-4-yl, thia-zolyl, imidazolyl or furanyl,

Aryl1 is pyridyl, phenyl or phenyl substituted by R18 and/or R19,

Aryl2 is pyridyl, phenyl, phenyl substituted by R18 and/or R19, 2-oxo-2H-chromen-7-yl or 4-(1,2,3-thiadiazol-4-yl)phenyl,

n is an integer from 1 to 4,

m is an integer from 1 to 4, or a pharmaceutically acceptable salt thereof, and (ii) one or more differentiation inducing agents.

- **34.** A method for treating neoplasms of lymphoid cells in a mammal, including: administering to said mammal therapeutically effective amounts of
- (i) a compound of formula 2

in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a benzene derivative of formula (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine, R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is 1-4C-alkyl, -S(O)₂-R10, -S(O)₂-(CH₂)_n-R11, -(CH₂)_m-S(O)₂-R12, -C(O)R13, -C(O)-(CH₂)_n-R14, -(CH₂)_m-C(O)-R15, Hetaryl, Aryl1 or 1-4C-alkyl-Aryl2,

R10 is 1-4C-alkyl, 5-dimethylaminonaphthalin-1-yl, -N(R16)R17, phenyl or phenyl substituted by R18 and/or R19,

R11 is -N(R16)R17,

R12 is -N(R16)R17,

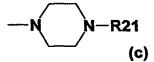
R13 is 1-4C-alkyl, hydroxycarbonyl-1-4C-alkyl, phenyl, pyridyl, 4-ethyl-piperazin-2,3-dion-1-yl or -N(R16)R17,

R14 is -N(R16)R17,

R15 is -N(R16)R17, phenyl, phenyl substituted by R18 and/or R19 and/or R20,

R16 and R17 are independent from each other hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl,

3-7C-cycloalkylmethyl, phenyl or phenyl substituted by R18 and/or R19 and/or R20, or R16 and R17 together and with inclusion of the nitrogen atom to which they are bonded, form a 4-morpholinyl-, 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepino- or a 1-piperazinyl-ring of formula (c)



wherein

R21 is pyrid-4-yl, pyrid-4-ylmethyl, 1-4C-alkyl-dimethylamino, dimethylaminocarbonylmethyl, N-methyl-piperidin-4-yl, 4-morpholino-ethyl or tetrahydrofuran-2-ylmethyl,

R18 is halogen, nitro, cyano, carboxyl, 1-4C-alkyl, trifluoromethyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, amino, mono-or di-1-4C-alkylamino, aminocarbonyl 1-4C-alkylcarbonylamino or mono-or di-1-4C-alkylaminocarbonyl,

R19 is halogen, amino, nitro, 1-4C-alkyl or 1-4C-alkoxy,

R20 is halogen,

Hetaryl is pyrimidin-2-yl, thieno-[2,3-d]pyrimidin-4-yl, 1-methyl-1H-pyrazolo-[3,4-d]pyrimidin-4-yl, thia-zolyl, imidazolyl or furanyl,

Aryl1 is pyridyl, phenyl or phenyl substituted by R18 and/or R19,

Aryl2 is pyridyl, phenyl, phenyl substituted by R18 and/or R19, 2-oxo-2H-chromen-7-yl or 4-(1,2,3-thiadiazol-4-yl)phenyl,

n is an integer from 1 to 4,

m is an integer from 1 to 4,

or a pharmaceutically acceptable salt thereof,

and (ii) an agent effective in raising intracellular concentrations of cAMP or a stable analogue thereof.

35. A method according to any of the claims 31, 32, 33 or 34, wherein the compound of formula 2 is selected from

(4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-[1-(toluene-4-sulfonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,

(4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-(1-methanesulfonyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,

(4aS,8aR)-2-(1-Acetyl-piperidin-4-yl)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,

5-{4-[(4aS,8aR)-4-(3,4-Diethoxy-phenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-5-oxo-pentanoic acid,

(4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-[1-(1-pyridin-4-yl-methanoyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,

4-[(4aS,8aR)-4-(3,4-Diethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidine-1-carboxylic acid tert-butylamide,

4-[(4aS,8aR)-4-(3,4-Diethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidine-1-carboxylic acid phenylamide,

4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidine-1-carboxylic acid tert-butylamide,

(cis)-4-[4-(7-Methoxy-2,2-dimethyl-2,3-dihydro-benzofuran-4-yl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phtha-lazin-2-yl]-piperidine-1-carboxylic acid tert-butylamide,

(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(5-dimethylamino-naphthalene-1-sulfonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,

(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(4-nitro-phenyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,

(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-pyridin-4-ylmethyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,

(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(morpholine-4-carbonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,

(4aS,8aR)-2-{1-[2-(4-Amino-3,5-dichloro-phenyl)-2-oxo-ethyl]-piperidin-4-yl}-4-(3,4-dimethoxy-phenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,

 $\label{eq:continuous} 4-(3,4-Dimethoxyphenyl)-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-piperidin-4-yl]-4a,5,8,8a-te-trahydro-2H-naphthalen-1-one,$

(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-thieno[2,3-d]pyrimidin-4-yl-piperidin-4-yl)-4a,5,8,8a-tetra-hydro-2H-phthalazin-1-one,

- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-pyrimidin-2-yl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phtha-lazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(2-oxo-2H-chromen-7-ylmethyl)-piperidin-4-yl]-4a,5,8,8a-te-trahydro-2H-phthalazin-1-one,
- 4-(3,4-Dimethoxyphenyl)-2-(1-isopropyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one, (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(2-morpholin-4-yl-2-oxo-ethyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-phenethyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-[1-(morpholine-4-carbonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-pyridin-3-ylmethyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxy-phenyl)-2-(1-pyridin-2-ylmethyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-[1-(2-morpholin-4-yl-ethanoyl)-piperidin-4-yl]-4a,5,8,8a-tetrahy-dro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-(1-{2-[4-(2-dimethylamino-ethyl)-piperazin-1-yl]-ethanoyl}-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- 2-{4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-N-isopropyl-acetamide,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(4-1,2,3-thiadiazol-4-yl-benzyl)-piperidin-4-yl]-4a,5,8,8a-tetra-hydro-2H-phthalazin-1-one,
- 1-(1-{4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-methanoyl)-4-ethyl-piperazine-2,3-dione,
- 4-(2-[4-[(4aS,8aR)-4-(3,4-Dimethoxy-phenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-ethanoylamino)-benzoic acid ethyl ester and
- 2-{4-[(4aS, 8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-acetamide,
- or a pharmaceutically acceptable salt thereof.
- **36.** A method according to any of the claims 31, 32, 33 or 34, wherein the compound of formula 2 is (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-pyrimidin-2-yl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one or a pharmaceutically acceptable salt thereof.
- **37.** A method according to any of the claims 31, 32, 33 or 34, wherein the compound of formula 2 is (4aS,8aR)-4-(3,4-Dimethoxy-phenyl)-2-(1-pyridin-2-ylmethyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one or a pharmaceutically acceptable salt thereof.

- 38. A method according to any of the claims 31, 32, 33 or 34, wherein the compound of formula 2 is 2-{4-[(4aS, 8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-acetamide or a pharmaceutically acceptable salt thereof.
- **39.** A method of treating neoplasms of lymphoid cells in a mammal, comprising administering to said mammal a therapeutically effective amount of a compound selected from

N-(3,5-dichloropyrid-4-yl)-3-cyclopentyloxy-4-methoxybenzamide [INN: PICLAMILAST],

3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST], 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide),

3-[3-(cyclopentyloxy)-4-methoxybenzyl]-6-(ethylamino)-8-isopropyl-3H-purine [Research Code: V-11294A],

N-[9-methyl-4-oxo-1-phenyl-3,4,6,7-tetrahydropyrrolo[3,2,1-jk][1,4]benzo-diazepin-3(R)-yl]pyridine-4-carboxamide [Research Code: Cl-1018],

3,7-dihydro-3-(4-chlorophenyl)-1-propyl-1H-purine-2,6-dione [INN: AROFYLLINE],

N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281],

N-(3,5-dichloropyridin-4-yl)-2-[5-fluoro-1-(4-fluorobenzyl)-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-343],

Tetrahydro-5-[4-methoxy-3-[(1S,2S,4R)-2-norbornyloxy]phenyl]-2(1H)-pyrimidone [INN: ATIZORAM]; ß-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1,3-dioxo-2H-isoindole-2-propanamide [Research Code: CDC-801],

Methanesulfonic acid 2-(2,4-dichlorophenylcarbonyl)-3-ureidobenzo-furan-6-yl ester [INN: LIRIMI-LAST],

3,5-dichloro-4-[8-methoxy-2-(trifluoromethyl)quinolin-5-ylcarbox-amido]pyridine-1-oxide [Research Code: SCH-351591],

cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast], the compounds with the research codes CDC-998, D-4396, IC-485, CC-1088 and KW4490, or a pharmaceutically acceptable salt thereof.

- **40.** A method for treating neoplasms of lymphoid cells in a mammal, including: administering to said mammal therapeutically effective amounts of
- (i) a compound selected from

N-(3,5-dichloropyrid-4-yl)-3-cyclopentyloxy-4-methoxybenzamide [INN: PICLAMILAST],

- 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST], 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide),
- 3-[3-(cyclopentyloxy)-4-methoxybenzyl]-6-(ethylamino)-8-isopropyl-3H-purine [Research Code: V-11294A],

N-[9-methyl-4-oxo-1-phenyl-3,4,6,7-tetrahydropyrrolo[3,2,1-jk][1,4]benzo-diazepin-3(R)-yl]pyridine-4-carboxamide [Research Code: CI-1018],

3,7-dihydro-3-(4-chlorophenyl)-1-propyl-1H-purine-2,6-dione [INN: AROFYLLINE],

N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281],

N-(3,5-dichloropyridin-4-yl)-2-[5-fluoro-1-(4-fluorobenzyl)-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-343],

Tetrahydro-5-[4-methoxy-3-[(1S,2S,4R)-2-norbornyloxy]phenyl]-2(1H)-pyrimidone [INN: ATIZORAM]; ß-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1,3-dioxo-2H-isoindole-2-propanamide [Research Code: CDC-801],

Methanesulfonic acid 2-(2,4-dichlorophenylcarbonyl)-3-ureidobenzo-furan-6-yl ester [INN: LIRIMI-LAST],

3,5-dichloro-4-[8-methoxy-2-(trifluoromethyl)quinolin-5-ylcarbox-amido]pyridine-1-oxide [Research Code: SCH-351591],

cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast], the compounds with the research codes CDC-998, D-4396, IC-485, CC-1088 and KW4490, or a pharmaceutically acceptable salt thereof,

and (ii) one or more differentiation inducing agents and/or an agent effective in raising intracellular concentrations of cAMP or a stable analogue thereof.

- **41.** A method for treating neoplasms of lymphoid cells in a mammal, including: administering to said mammal therapeutically effective amounts of
- (i) a compound selected from

N-(3,5-dichloropyrid-4-yl)-3-cyclopentyloxy-4-methoxybenzamide [INN: PICLAMILAST],

3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST], 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-

Oxide)

3-[3-(cyclopentyloxy)-4-methoxybenzyl]-6-(ethylamino)-8-isopropyl-3H-purine [Research Code: V-11294A],

N-[9-methyl-4-oxo-1-phenyl-3,4,6,7-tetrahydropyrrolo[3,2,1-jk][1,4]benzo-diazepin-3(R)-yl]pyridine-4-carboxamide [Research Code: Cl-1018],

3,7-dihydro-3-(4-chlorophenyl)-1-propyl-1H-purine-2,6-dione [INN: AROFYLLINE],

N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281],

N-(3,5-dichloropyridin-4-yl)-2-[5-fluoro-1-(4-fluorobenzyl)-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-343],

Tetrahydro-5-[4-methoxy-3-[(1S,2S,4R)-2-norbornyloxy]phenyl]-2(1H)-pyrimidone [INN: ATIZORAM]; ß-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1,3-dioxo-2H-isoindole-2-propanamide [Research Code: CDC-801],

Methanesulfonic acid 2-(2,4-dichlorophenylcarbonyl)-3-ureidobenzo-furan-6-yl ester [INN: LIRIMI-LAST],

3,5-dichloro-4-[8-methoxy-2-(trifluoromethyl)quinolin-5-ylcarbox-amido]pyridine-1-oxide [Research Code: SCH-351591],

cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast], the compounds with the research codes CDC-998, D-4396, IC-485, CC-1088 and KW4490, or a pharmaceutically acceptable salt thereof,

and (ii) one or more differentiation inducing agents.

- **42.** A method for treating neoplasms of lymphoid cells in a mammal, including: administering to said mammal therapeutically effective amounts of
- (i) a compound selected from
- N-(3,5-dichloropyrid-4-yl)-3-cyclopentyloxy-4-methoxybenzamide [INN: PICLAMILAST],
- 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST],
- 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide),
- 3-[3-(cyclopentyloxy)-4-methoxybenzyl]-6-(ethylamino)-8-isopropyl-3H-purine [Research Code: V-11294A],
- N-[9-methyl-4-oxo-1-phenyl-3,4,6,7-tetrahydropyrrolo[3,2,1-jk][1,4]benzo-diazepin-3(R)-yl]pyridine-4-carboxamide [Research Code: CI-1018],
- 3,7-dihydro-3-(4-chlorophenyl)-1-propyl-1H-purine-2,6-dione [INN: AROFYLLINE],
- N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281],
- N-(3,5-dichloropyridin-4-yl)-2-[5-fluoro-1-(4-fluorobenzyl)-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-343],
- Tetrahydro-5-[4-methoxy-3-[(1S,2S,4R)-2-norbornyloxy]phenyl]-2(1H)-pyrimidone [INN: ATIZORAM]; ß-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1,3-dioxo-2H-isoindole-2-propanamide [Research Code: CDC-801],
- Methanesulfonic acid 2-(2,4-dichlorophenylcarbonyl)-3-ureidobenzo-furan-6-yl ester [INN: LIRIMI-LAST],
- 3,5-dichloro-4-[8-methoxy-2-(trifluoromethyl)quinolin-5-ylcarbox-amido]pyridine-1-oxide [Research Code: SCH-351591],
- cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast], the compounds with the research codes CDC-998, D-4396, IC-485, CC-1088 and KW4490, or a pharmaceutically acceptable salt thereof,
- and (ii) an agent effective in raising intracellular concentrations of cAMP or a stable analogue thereof.
- **43.** A method according to any of the claims 39, 40, 41 or 42, wherein the compound of component (i) is selected from

or a pharmaceutically acceptable salt thereof.

44. A method according to any of the claims 39, 40, 41 or 42, wherein the compound of component (i) is selected from

N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281],

cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast], 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST] and

3-cyclopropylmethoxy-4-diffuoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide),

or a pharmaceutically acceptable salt thereof.

45. A method according to any of the claims 39, 40, 41 or 42, wherein the compound of component (i) is

3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST] and 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide),

or a pharmaceutically acceptable salt thereof.

46. A method according to any of the claims 39, 40, 41 or 42, wherein the compound of component (i) is

3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST] or a pharmaceutically acceptable salt thereof.

47. A method according to any of the claims 39, 40, 41 or 42, wherein the compound of component (i) is

3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide) or a pharmaceutically acceptable salt thereof.

48. A method according to any of the claims 39, 40, 41 or 42, wherein the compound of component (i) is

N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281] or a pharmaceutically acceptable salt thereof.

49. A method according to any of the claims 39, 40, 41 or 42, wherein the compound of component (i) is

cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast] or a pharmaceutically acceptable salt thereof.

50. A treatment combination for neoplasms of lymphoid cells, comprising: therapeutically effective amounts of

(i) a compound of formula 1

in which

R1 and R2 are both hydrogen or together form an additional bond,

A represents S (sulfur), S(O) (sulfoxide) or S(O)₂ (sulfone),

Ar represents a benzene derivative of formula (a) or (b)

wherein

- R3 is halogen, 1-4C-alkoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine.
- R4 is halogen, 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,
- R5 is halogen, 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkyl and

R7 is hydrogen or 1-4C-alkyl,

or wherein

R6 and R7 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

or a pharmaceutically acceptable salt thereof,

and (ii) one or more differentiation inducing agents and/or an agent effective in raising intracellular concentrations of cAMP or a stable analogue of cAMP.

- **51.** A treatment combination for neoplasms of lymphoid cells, comprising: therapeutically effective amounts of
- (i) a compound of formula 1

in which

R1 and R2 are both hydrogen or together form an additional bond,

- A represents S (sulfur), S(O) (sulfoxide) or S(O)₂ (sulfone),
- Ar represents a benzene derivative of formula (a) or (b)

- R3 is halogen, 1-4C-alkoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,
- R4 is halogen, 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is halogen, 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkyl and

R7 is hydrogen or 1-4C-alkyl,

or wherein

R6 and R7 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

or a pharmaceutically acceptable salt thereof, and (ii) one or more differentiation inducing agents.

- **52.** A treatment combination for neoplasms of lymphoid cells, comprising: therapeutically effective amounts of
- (i) a compound of formula 1

in which

R1 and R2 are both hydrogen or together form an additional bond,

A represents S (sulfur), S(O) (sulfoxide) or S(O)₂ (sulfone),

Ar represents a benzene derivative of formula (a) or (b)

- R3 is halogen, 1-4C-alkoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,
- R4 is halogen, 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,
- R5 is halogen, 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,
- R6 is 1-4C-alkyl and
- R7 is hydrogen or 1-4C-alkyl,

or wherein

R6 and R7 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

or a pharmaceutically acceptable salt thereof,

and (ii) an agent effective in raising intracellular concentrations of cAMP or a stable analogue of cAMP.

- **53.** A treatment combination according to any of the claims 50, 51 or 52, wherein the compound of formula 1 is selected from
- (cis)-4-(2,3-Dihydro-2,2-dimethyl-7-methoxybenzofuran-4-yl)-2-(tetrahydrothiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (cis)-4-(3,4-Dimethoxyphenyl)-2-(1,1-dioxohexahydro-1l⁶-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (cis)-4-(3,4-Dimethoxyphenyl)-2-(1-oxo-hexahydro-1l⁴-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phtha-lazin-1-one,
- (cis)-4-(3-Chloro-4-methoxyphenyl)-2-(tetrahydrothiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one.
- (cis)-4-(3-Chloro-4-methoxyphenyl)-2-(1-oxo-hexahydro-1i⁴-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,.
- (cis)-4-(3,4-Diethoxyphenyl)-2-(1,1-dioxohexahydro-11⁶-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phtha-lazin-1-one,
- (cis)-4-(2,3-Dihydro-2,2-dimethyl-7-methoxybenzofuran-4-yl)-2-(1,1-dioxohexahydro-1l⁶-thiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aR,8aS)-(cis)-4-(3,4-Dimethoxyphenyl)-2-(1,1-dioxohexahydro-1l⁶-thiopyran-4-yl)-4a,5,8,8a-tetrahy-dro-2H-phthalazin-1-one,
- (4aS,8aR)-(cis)-4-(3,4-Dimethoxyphenyl)-2-(1,1-dioxohexahydro-1l⁶-thiopyran-4-yl)-4a,5,8,8a-tetrahy-dro-2H-phthalazin-1-one and
- (cis)-4-(3-Cyclopentyloxy-4-methoxyphenyl)-2-(1,1-dioxohexahydro-1l⁶-thiopyran-4-yl)-4a,5,8,8a-tetra-hydro-2H-phthalazin-1-one,
- or a pharmaceutically acceptable salt thereof.

54. A treatment combination according to any of the claims 50, 51 or 52, wherein the compound of formula 1 is selected from

(cis)-4-(2,3-Dihydro-2,2-dimethyl-7-methoxybenzofuran-4-yl)-2-(tetrahydrothiopyran-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,

(4aS,8aR)-(cis)-4-(3,4-Dimethoxyphenyl)-2-(1,1-dioxohexahydro-1l⁶-thiopyran-4-yl)-4a,5,8,8a-tetrahy-dro-2H-phthalazin-1-one and

(cis)-4-(3-Cyclopentyloxy-4-methoxyphenyl)-2-(1,1-dioxohexahydro-1l⁶-thiopyran-4-yl)-4a,5,8,8a-tetra-hydro-2H-phthalazin-1-one,

or a pharmaceutically acceptable salt thereof.

55. A treatment combination for neoplasms of lymphoid cells, comprising: therapeutically effective amounts of

(i) a compound of formula 2

in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a benzene derivative of formula (a) or (b)

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine, R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is 1-4C-alkyl, -S(O)₂-R10, -S(O)₂-(CH₂)_n-R11, -(CH₂)_m-S(O)₂-R12, -C(O)R13, -C(O)-(CH₂)_n-R14, -(CH₂)_m-C(O)-R15, Hetaryl, Aryl1 or 1-4C-alkyl-Aryl2,

R10 is 1-4C-alkyl, 5-dimethylaminonaphthalin-1-yl, -N(R16)R17, phenyl or phenyl substituted by R18 and/or R19,

R11 is -N(R16)R17,

R12 is -N(R16)R17,

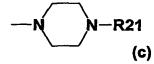
R13 is 1-4C-alkyl, hydroxycarbonyl-1-4C-alkyl, phenyl, pyridyl, 4-ethyl-piperazin-2,3-dion-1-yl or -N(R16)R17,

R14 is -N(R16)R17,

R15 is -N(R16)R17, phenyl, phenyl substituted by R18 and/or R19 and/or R20,

R16 and R17 are independent from each other hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl,

3-7C-cycloalkylmethyl, phenyl or phenyl substituted by R18 and/or R19 and/or R20, or R16 and R17 together and with inclusion of the nitrogen atom to which they are bonded, form a 4-morpholinyl-, 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepino- or a 1-piperazinyl-ring of formula (c)



wherein

R21 is pyrid-4-yl, pyrid-4-ylmethyl, 1-4C-alkyl-dimethylamino, dimethylaminocarbonylmethyl, N-methyl-piperidin-4-yl, 4-morpholino-ethyl or tetrahydrofuran-2-ylmethyl,

R18 is halogen, nitro, cyano, carboxyl, 1-4C-alkyl, trifluoromethyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, amino, mono-or di-1-4C-alkylamino, aminocarbonyl 1-4C-alkylamino or mono-or di-1-4C-alkylaminocarbonyl,

R19 is halogen, amino, nitro, 1-4C-alkyl or 1-4C-alkoxy,

R20 is halogen,

Hetaryl is pyrimidin-2-yl, thieno-[2,3-d]pyrimidin-4-yl, 1-methyl-1H-pyrazolo-[3,4-d]pyrimidin-4-yl, thia-zolyl, imidazolyl or furanyl,

Aryl1 is pyridyl, phenyl or phenyl substituted by R18 and/or R19,

Aryl2 is pyridyl, phenyl, phenyl substituted by R18 and/or R19, 2-oxo-2H-chromen-7-yl or 4-(1,2,3-thiadiazol-4-yl)phenyl,

n is an integer from 1 to 4,

m is an integer from 1 to 4,

or a pharmaceutically acceptable salt thereof,

and (ii) one or more differentiation inducing agents and/or an agent effective in raising intracellular concentrations of cAMP or a stable analogue of cAMP.

56. A treatment combination for neoplasms of lymphoid cells, comprising: therapeutically effective amounts of

(i) a compound of formula 2

in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a benzene derivative of formula (a) or (b)

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine, R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is 1-4C-alkyl, $-S(O)_2$ -R10, $-S(O)_2$ -(CH₂)_n-R11, $-(CH_2)_m$ -S(O)₂-R12, -C(O)-R13, -C(O)-(CH₂)_n-R14, $-(CH_2)_m$ -C(O)-R15, Hetaryl, Aryl1 or 1-4C-alkyl-Aryl2,

R10 is 1-4C-alkyl, 5-dimethylaminonaphthalin-1-yl, -N(R16)R17, phenyl or phenyl substituted by R18 and/or R19,

R11 is -N(R16)R17,

R12 is -N(R16)R17,

R13 is 1-4C-alkyl, hydroxycarbonyl-1-4C-alkyl, phenyl, pyridyl, 4-ethyl-piperazin-2,3-dion-1-yl or -N(R16)R17,

R14 is -N(R16)R17,

R15 is -N(R16)R17, phenyl, phenyl substituted by R18 and/or R19 and/or R20,

R16 and R17 are independent from each other hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl,

3-7C-cycloalkylmethyl, phenyl or phenyl substituted by R18 and/or R19 and/or R20, or R16 and R17 together and with inclusion of the nitrogen atom to which they are bonded, form a 4-morpholinyl-, 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepino- or a 1-piperazinyl-ring of formula (c)

wherein

R21 is pyrid-4-yl, pyrid-4-ylmethyl, 1-4C-alkyl-dimethylamino, dimethylaminocarbonylmethyl, N-methyl-piperidin-4-yl, 4-morpholino-ethyl or tetrahydrofuran-2-ylmethyl,

R18 is halogen, nitro, cyano, carboxyl, 1-4C-alkyl, trifluoromethyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, amino, mono-or di-1-4C-alkylamino, aminocarbonyl 1-4C-alkylcarbonylamino or mono-or di-1-4C-alkylaminocarbonyl,

R19 is halogen, amino, nitro, 1-4C-alkyl or 1-4C-alkoxy,

R20 is halogen,

Hetaryl is pyrimidin-2-yl, thieno-[2,3-d]pyrimidin-4-yl, 1-methyl-1H-pyrazolo-[3,4-d]pyrimidin-4-yl, thia-zolyl, imidazolyl or furanyl,

Aryl1 is pyridyl, phenyl or phenyl substituted by R18 and/or R19,

Aryl2 is pyridyl, phenyl, phenyl substituted by R18 and/or R19, 2-oxo-2H-chromen-7-yl or 4-(1,2,3-thiadiazol-4-yl)phenyl,

n is an integer from 1 to 4,

m is an integer from 1 to 4,

or a pharmaceutically acceptable salt thereof,

and (ii) one or more differentiation inducing agents.

- **57.** A treatment combination for neoplasms of lymphoid cells, comprising: therapeutically effective amounts of
- (i) a compound of formula 2

in which

R1 and R2 are both hydrogen or together form an additional bond,

R3 represents a benzene derivative of formula (a) or (b)

wherein

R4 is 1-4C-alkoxy or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R5 is 1-8C-alkoxy, 3-7C-cycloalkoxy, 3-7C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R6 is 1-4C-alkoxy, 3-5C-cycloalkoxy, 3-5C-cycloalkylmethoxy, or 1-4C-alkoxy which is completely or predominantly substituted by fluorine,

R7 is 1-4C-alkyl and

R8 is hydrogen or 1-4C-alkyl,

or wherein

R7 and R8 together and with inclusion of the two carbon atoms, to which they are bonded, form a spiro-linked 5-, 6- or 7-membered hydrocarbon ring, optionally interrupted by an oxygen or sulphur atom,

R9 is 1-4C-alkyl, -S(O)₂-R10, -S(O)₂-(CH₂)_n-R11, -(CH₂)_m-S(O)₂-R12, -C(O)R13, -C(O)-(CH₂)_n-R14, -(CH₂)_m-C(O)-R15, Hetaryl, Aryl1 or 1-4C-alkyl-Aryl2,

R10 is 1-4C-alkyl, 5-dimethylaminonaphthalin-1-yl, -N(R16)R17, phenyl or phenyl substituted by R18 and/or R19,

R11 is -N(R16)R17,

R12 is -N(R16)R17,

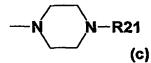
R13 is 1-4C-alkyl, hydroxycarbonyl-1-4C-alkyl, phenyl, pyridyl, 4-ethyl-piperazin-2,3-dion-1-yl or -N(R16)R17,

R14 is -N(R16)R17,

R15 is -N(R16)R17, phenyl, phenyl substituted by R18 and/or R19 and/or R20,

R16 and R17 are independent from each other hydrogen, 1-7C-alkyl, 3-7C-cycloalkyl,

3-7C-cycloalkylmethyl, phenyl or phenyl substituted by R18 and/or R19 and/or R20, or R16 and R17 together and with inclusion of the nitrogen atom to which they are bonded, form a 4-morpholinyl-, 1-pyrrolidinyl-, 1-piperidinyl-, 1-hexahydroazepino- or a 1-piperazinyl-ring of formula (c)



wherein

R21 is pyrid-4-yl, pyrid-4-ylmethyl, 1-4C-alkyl-dimethylamino, dimethylaminocarbonylmethyl, N-methyl-piperidin-4-yl, 4-morpholino-ethyl or tetrahydrofuran-2-ylmethyl,

R18 is halogen, nitro, cyano, carboxyl, 1-4C-alkyl, trifluoromethyl, 1-4C-alkoxy, 1-4C-alkoxycarbonyl, amino, mono-or di-1-4C-alkylamino, aminocarbonyl 1-4C-alkylamino or mono-or di-1-4C-alkylaminocarbonyl,

R19 is halogen, amino, nitro, 1-4C-alkyl or 1-4C-alkoxy,

R20 is halogen,

- Hetaryl is pyrimidin-2-yl, thieno-[2,3-d]pyrimidin-4-yl, 1-methyl-1H-pyrazolo-[3,4-d]pyrimidin-4-yl, thia-zolyl, imidazolyl or furanyl,
- Aryl1 is pyridyl, phenyl or phenyl substituted by R18 and/or R19,
- Aryl2 is pyridyl, phenyl, phenyl substituted by R18 and/or R19, 2-oxo-2H-chromen-7-yl or 4-(1,2,3-thiadiazol-4-yl)phenyl,
- n is an integer from 1 to 4,
- m is an integer from 1 to 4,
- or a pharmaceutically acceptable salt thereof,
- and (ii) an agent effective in raising intracellular concentrations of cAMP or a stable analogue of cAMP.
- **58.** A treatment combination according to any of the claims 55, 56 or 57, wherein the compound of formula 2 is selected from
- (4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-[1-(toluene-4-sulfonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-(1-methanesulfonyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-2-(1-Acetyl-piperidin-4-yl)-4-(3,4-diethoxyphenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one.
- 5-{4-[(4aS,8aR)-4-(3,4-Diethoxy-phenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-5-oxo-pentanoic acid,
- (4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-[1-(1-pyridin-4-yl-methanoyl)-píperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- 4-[(4aS,8aR)-4-(3,4-Diethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidine-1-carboxylic acid tert-butylamide,
- 4-[(4aS,8aR)-4-(3,4-Diethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidine-1-carboxylic acid phenylamide,
- 4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidine-1-carboxylic acid tert-butylamide,
- (cis)-4-[4-(7-Methoxy-2,2-dimethyl-2,3-dihydro-benzofuran-4-yl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phtha-lazin-2-yl]-piperidine-1-carboxylic acid tert-butylamide,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(5-dimethylamino-naphthalene-1-sulfonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(4-nitro-phenyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-pyridin-4-ylmethyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(morpholine-4-carbonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,

- (4aS,8aR)-2-{1-[2-(4-Amino-3,5-dichloro-phenyl)-2-oxo-ethyl]-piperidin-4-yl}-4-(3,4-dimethoxy-phenyl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- 4-(3,4-Dimethoxyphenyl)-2-[1-(1-methyl-1H-pyrazolo[3,4-d]pyrimidin-4-yl)-piperidin-4-yl]-4a,5,8,8a-te-trahydro-2H-naphthalen-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-thieno[2,3-d]pyrimidin-4-yl-piperidin-4-yl)-4a,5,8,8a-tetra-hydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-pyrimidin-2-yl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phtha-lazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(2-oxo-2H-chromen-7-ylmethyl)-piperidin-4-yl]-4a,5,8,8a-te-trahydro-2H-phthalazin-1-one,
- 4-(3,4-Dimethoxyphenyl)-2-(1-isopropyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one, (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(2-morpholin-4-yl-2-oxo-ethyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-phenethyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-[1-(morpholine-4-carbonyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-pyridin-3-ylmethyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Dimethoxy-phenyl)-2-(1-pyridin-2-ylmethyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- (4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-[1-(2-morpholin-4-yl-ethanoyl)-piperidin-4-yl]-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,
- $\label{lem:condition} $$(4aS,8aR)-4-(3,4-Diethoxyphenyl)-2-(1-\{2-[4-(2-dimethylamino-ethyl)-piperazin-1-yl]-ethanoyl\}-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one,$
- 2-{4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-N-isopropyl-acetamide,
- (4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-[1-(4-1,2,3-thiadiazol-4-yl-benzyl)-piperidin-4-yl]-4a,5,8,8a-tetra-hydro-2H-phthalazin-1-one,
- 1-(1-{4-[(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-methanoyl)-4-ethyl-piperazine-2,3-dione,
- 4-(2-{4-[(4aS,8aR)-4-(3,4-Dimethoxy-phenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-ethanoylamino)-benzoic acid ethyl ester and
- 2-{4-[(4aS, 8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-acetamide,
- or a pharmaceutically acceptable salt thereof.
- **59.** A treatment combination according to any of the claims 55, 56 or 57, wherein the compound of formula 2 is

(4aS,8aR)-4-(3,4-Dimethoxyphenyl)-2-(1-pyrimidin-2-yl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phtha-lazin-1-one or a pharmaceutically acceptable salt thereof.

60. A treatment combination according to any of the claims 55, 56 or 57, wherein the compound of formula 2 is

(4aS,8aR)-4-(3,4-Dimethoxy-phenyl)-2-(1-pyridin-2-ylmethyl-piperidin-4-yl)-4a,5,8,8a-tetrahydro-2H-phthalazin-1-one or a pharmaceutically acceptable salt thereof.

61. A treatment combination according to any of the claims 55, 56 or 57, wherein the compound of formula 2 is

2-{4-[(4aS, 8aR)-4-(3,4-Dimethoxyphenyl)-1-oxo-4a,5,8,8a-tetrahydro-1H-phthalazin-2-yl]-piperidin-1-yl}-acetamide or a pharmaceutically acceptable salt thereof.

- **62.** A treatment combination for neoplasms of lymphoid cells, comprising: therapeutically effective amounts of
- (i) a compound selected from

N-(3,5-dichloropyrid-4-yl)-3-cyclopentyloxy-4-methoxybenzamide [INN: PICLAMILAST],

3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST],

3-cyclopropylmethoxy-4-diffuoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roffumilast-N-Oxide),

3-[3-(cyclopentyloxy)-4-methoxybenzyl]-6-(ethylamino)-8-isopropyl-3H-purine [Research Code: V-11294A],

N-[9-methyl-4-oxo-1-phenyl-3,4,6,7-tetrahydropyrrolo[3,2,1-jk][1,4]benzo-diazepin-3(R)-yl]pyridine-4-carboxamide [Research Code: Cl-1018],

3,7-dihydro-3-(4-chlorophenyl)-1-propyl-1H-purine-2,6-dione [INN: AROFYLLINE],

N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281],

N-(3,5-dichloropyridin-4-yl)-2-[5-fluoro-1-(4-fluorobenzyl)-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-343],

Tetrahydro-5-[4-methoxy-3-[(1S,2S,4R)-2-norbornyloxy]phenyl]-2(1H)-pyrimidone [INN: ATIZORAM]; ß-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1,3-dioxo-2H-isoindole-2-propanamide [Research Code: CDC-801],

Methanesulfonic acid 2-(2,4-dichlorophenylcarbonyl)-3-ureidobenzo-furan-6-yl ester [INN: LIRIMI-LAST],

3,5-dichloro-4-[8-methoxy-2-(trifluoromethyl)quinolin-5-ylcarbox-amido]pyridine-1-oxide [Research Code: SCH-351591],

cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast], the compounds with the research codes CDC-998, D-4396, IC-485, CC-1088 and KW4490, or a pharmaceutically acceptable salt thereof,

and (ii) one or more differentiation inducing agents and/or an agent effective in raising intracellular concentrations of cAMP or a stable analogue of cAMP.

- **63.** A treatment combination for neoplasms of lymphoid cells, comprising: therapeutically effective amounts of
- (i) a compound selected from

N-(3,5-dichloropyrid-4-yl)-3-cyclopentyloxy-4-methoxybenzamide [INN: PICLAMILAST],

3-cyclopropylmethoxy-4-diffuoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST], 3-cyclopropylmethoxy-4-diffuoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide),

3-[3-(cyclopentyloxy)-4-methoxybenzyl]-6-(ethylamino)-8-isopropyl-3H-purine [Research Code: V-11294A],

N-[9-methyl-4-oxo-1-phenyl-3,4,6,7-tetrahydropyrrolo[3,2,1-jk][1,4]benzo-diazepin-3(R)-yl]pyridine-4-carboxamide [Research Code: CI-1018],

3,7-dihydro-3-(4-chlorophenyl)-1-propyl-1H-purine-2,6-dione [INN: AROFYLLINE],

N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281],

N-(3,5-dichloropyridin-4-yl)-2-[5-fluoro-1-(4-fluorobenzyl)-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-343],

Tetrahydro-5-[4-methoxy-3-[(1S,2S,4R)-2-norbornyloxy]phenyl]-2(1H)-pyrimidone [INN: ATIZORAM]; ß-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1,3-dioxo-2H-isoindole-2-propanamide [Research Code: CDC-801],

Methanesulfonic acid 2-(2,4-dichlorophenylcarbonyl)-3-ureidobenzo-furan-6-yl ester [INN: LIRIMI-LAST],

3,5-dichloro-4-[8-methoxy-2-(trifluoromethyl)quinolin-5-ylcarbox-amido]pyridine-1-oxide [Research Code: SCH-351591],

cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast], the compounds with the research codes CDC-998, D-4396, IC-485, CC-1088 and KW4490, or a pharmaceutically acceptable salt thereof,

and (ii) one or more differentiation inducing agents.

- **64.** A treatment combination for neoplasms of lymphoid cells, comprising: therapeutically effective amounts of
- (i) a compound selected from

N-(3,5-dichloropyrid-4-yl)-3-cyclopentyloxy-4-methoxybenzamide [INN: PICLAMILAST], 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST], 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide),

3-[3-(cyclopentyloxy)-4-methoxybenzyl]-6-(ethylamino)-8-isopropyl-3H-purine [Research Code: V-11294A],

N-[9-methyl-4-oxo-1-phenyl-3,4,6,7-tetrahydropyrrolo[3,2,1-jk][1,4]benzo-diazepin-3(R)-yl]pyridine-4-carboxamide [Research Code: CI-1018],

3,7-dihydro-3-(4-chlorophenyl)-1-propyl-1H-purine-2,6-dione [INN: AROFYLLINE],

N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281],

N-(3,5-dichloropyridin-4-yl)-2-[5-fluoro-1-(4-fluorobenzyl)-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-343],

Tetrahydro-5-[4-methoxy-3-[(1S,2S,4R)-2-norbornyloxy]phenyl]-2(1H)-pyrimidone [INN: ATIZORAM]; ß-[3-(cyclopentyloxy)-4-methoxyphenyl]-1,3-dihydro-1,3-dioxo-2H-isoindole-2-propanamide [Research Code: CDC-801],

Methanesulfonic acid 2-(2,4-dichlorophenylcarbonyl)-3-ureidobenzo-furan-6-yl ester [INN: LIRIMI-LAST],

3,5-dichloro-4-[8-methoxy-2-(trifluoromethyl)quinolin-5-ylcarbox-amido]pyridine-1-oxide [Research Code: SCH-351591],

cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast], the compounds with the research codes CDC-998, D-4396, IC-485, CC-1088 and KW4490, or a pharmaceutically acceptable salt thereof,

and (ii) an agent effective in raising intracellular concentrations of cAMP or a stable analogue of cAMP.

65. A treatment combination according to any of the claims 62, 63 or 64, wherein the compound of component (i) is selected from

N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281],

cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast], 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST] and

3-cyclopropylmethoxy-4-diffuoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide),

or a pharmaceutically acceptable salt thereof.

66. A treatment combination according to any of the claims 62, 63 or 64, wherein the compound of component (i) is selected from

3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST] and 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide),

or a pharmaceutically acceptable salt thereof.

- 67. A treatment combination according to any of the claims 62, 63 or 64, wherein the compound of component (i) is
- 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloropyrid-4-yl)-benzamide [INN: ROFLUMILAST] or a pharmaceutically acceptable salt thereof.
- **68.** A treatment combination according to any of the claims 62, 63 or 64, wherein the compound of component (i) is
- 3-cyclopropylmethoxy-4-difluoromethoxy-N-(3,5-dichloro-1-oxy-pyrid-4-yl)-benzamide (Roflumilast-N-Oxide) or a pharmaceutically acceptable salt thereof.
- **69.** A treatment combination according to any of the claims 62, 63 or 64, wherein the compound of component (i) is
- N-(3,5-dichloro-4-pyridinyl)-2-[1-(4-fluorobenzyl)-5-hydroxy-1H-indol-3-yl]-2-oxoacetamide [Research Code: AWD-12-281] or a pharmaceutically acceptable salt thereof.
- **70.** A treatment combination according to any of the claims 62, 63 or 64, wherein the compound of component (i) is cis-4-cyano-4-[3-cyclopentyloxy-4-methoxyphenyl]cyclohexane-1-carboxylic acid [INN: Cilomilast] or a pharmaceutically acceptable salt thereof.
- 71. The use according to any of the claims 2, 3, 5, 6, 8, 9, 11, 12, 13, 14, 16, 17, 19, 20, 21, 22, 23 or 24, wherein the differentiation inducing agent is selected from the group consisting of all trans retinoic acid, 13-cis-retinoic acid, CD437, rexinoids, histone deacetylase inhibitors, DNA methyltransferase inhibitors, hematopoietic growth factors, interferon α, interleukin 1, TRAIL, hexamethylene bisacetamide, cholecalciferol, arsenic trioxide, green tea catechin epigallocatechin-3-gallate, DNA topoisomerase II inhibitors, taraxinic acid, verticinone, PPAR-gamma agonists, antibodies versus CD19, CD20 or CD22, CD33-antibodies alone or as conjugate, alkylating cytostatika, purine analogs, cytosine- arabinosides, anticylines, vinca-alkaloids and glucocorticosteroids.
- 72. The use according to any of the claims 2, 3, 5, 6, 8, 9, 11, 12, 13, 14, 16, 17, 19, 20, 21, 22, 23 or 24, wherein the differentiation inducing agent is a histone deacetylase inhibitor.
- 73. The use according to any of the claims 2, 3, 5, 6, 8, 9, 11, 12, 13, 14, 16, 17, 19, 20, 21, 22, 23 or 24, wherein the differentiation inducing agent is all trans retinoic acid.
- 74. The use according to any of the claims 2, 4, 5, 6, 8, 10, 11, 12, 13, 14, 16, 18, 19, 20, 21, 22, 23 or 24, wherein the agent effective in raising intracellular concentrations of cAMP is selected from

the group consisting of prostaglandin E2, prostacyclin derivatives, dopamine, dobutamine, ß2-adrenoreceptor agonists, adenosine A1 receptor agonists, adenosine A2 receptor agonists and forskolin.

- 75. The method according to any of the claims 26, 27, 29, 30, 32, 33, 35, 36, 37, 38, 40, 41, 43, 44, 45, 46, 47, 48 or 49, wherein the differentiation inducing agent is selected from the group consisting of all trans retinoic acid, 13-cis-retinoic acid, CD437, rexinoids, histone deacetylase inhibitors, DNA methyltransferase inhibitors, hematopoietic growth factors, interferon α, interleukin 1, TRAIL, hexamethylene bisacetamide, cholecalciferol, arsenic trioxide, green tea catechin epigallocatechin-3-gallate, DNA topoisomerase II inhibitors, taraxinic acid, verticinone, PPAR-gamma agonists, antibodies versus CD19, CD20 or CD22, CD33-antibodies alone or as conjugate, alkylating cytostatika, purine analogs, cytosine- arabinosides, anticylines, vinca-alkaloids and glucocorticosteroids.
- **76.** The method according to any of the claims 26, 27, 29, 30, 32, 33, 35, 36, 37, 38, 40, 41, 43, 44, 45, 46, 47, 48 or 49, wherein the differentiation inducing agent is a histone deacetylase inhibitor.
- 77. The method according to any of the claims 26, 27, 29, 30, 32, 33, 35, 36, 37, 38, 40, 41, 43, 44, 45, 46, 47, 48 or 49, wherein the differentiation inducing agent is all trans retinoic acid.
- 78. The method according to any of the claims 26, 28, 29, 30, 32, 34, 35, 36, 37, 38, 40, 42, 43, 44, 45, 46, 47, 48 or 49, wherein the agent effective in raising intracellular concentrations of cAMP is selected from the group consisting of prostaglandin E2, prostacyclin derivatives, dopamine, dobutamine, ß2-adrenoreceptor agonists, adenosine A1 receptor agonists, adenosine A2 receptor agonists and forskolin.
- **79.** A treatment combination according to any of the claims 50, 51, 53, 54, 55, 56, 58, 59, 60, 61, 62, 63, 65, 66, 67, 68, 69 or 70, wherein the differentiation inducing agent is selected from the group consisting of all trans retinoic acid, 13-cis-retinoic acid, CD437, rexinoids, histone deacetylase inhibitors, DNA methyltransferase inhibitors, hematopoietic growth factors, interferon α, interleukin 1, TRAIL, hexamethylene bisacetamide, cholecalciferol, arsenic trioxide, green tea catechin epigallocatechin-3-gallate, DNA topoisomerase II inhibitors, taraxinic acid, verticinone, PPAR-gamma agonists, antibodies versus CD19, CD20 or CD22, CD33-antibodies alone or as conjugate, alkylating cytostatika, purine analogs, cytosine- arabinosides, anticylines, vinca-alkaloids and glucocorticosteroids.
- **80.** A treatment combination according to any of the claims 50, 52, 53, 54, 55, 57, 58, 59, 60, 61, 62, 64, 65, 66, 67, 68, 69 or 70, wherein the agent effective in raising intracellular concentrations of cAMP is selected from the group consisting of prostaglandin E2, prostacyclin derivatives, dopamine, dobutamine, ß2-adrenoreceptor agonists, adenosine A1 receptor agonists, adenosine A2 receptor agonists and forskolin.

- A treatment combination according to any of the claims 50, 51, 53, 54, 55, 56, 58, 59, 60, 61, 81. 62, 63, 65, 66, 67, 68, 69 or 70, wherein the differentiation inducing agent is a histone deacetylase inhibitor.
- 82. A treatment combination according to any of the claims 50, 51, 53, 54, 55, 56, 58, 59, 60, 61, 62, 63, 65, 66, 67, 68, 69 or 70, wherein the differentiation inducing agent is all trans retinoic acid.
- The use according to any of the claims 1-24 and 71-74, wherein the neoplasm of lymphoid 83. cells is leukemia.
- 84. The method according to any of the claims 25-49 and 75-78, wherein the neoplasm of lymphoid cells is leukemia.
- 85. The treatment combination according to any of the claims 50-70 and 79-82, wherein the neoplasm of lymphoid cells is leukemia.